In the office action of November 20, 2002, the following rejections were made:

(1) the election/restriction requirement was reaffirmed;

(2) claims 1-5, 7-8, 10, 12, 14, 40-46, 49, 51, 53, and 55-56 were rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Pat. No. 5,891,478 (hereinafter "'478");

(3) claims 1, 5, 7-9, 40, 46, 49, 50, and 52-56 were rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Pat. No. 4,765,980 (hereinafter "'980"); and

(4) claims 1, 7-13, 55, and 56 were rejected under the judicially created doctrine of obviousness-type double patenting over claims 1, 2, 6, 12, 18-21, 24, and 25 of U.S. Pat. No. 6,287,588 (hereinafter "'588").

ELECTION/RESTRICTION REQUIREMENT

It appears that the Examiner has withdrawn claims 6 and 47 from consideration, even though it lists several zinc salts (which was one of the groups elected under an election of species requirement). Clarification is requested. Please withdraw from consideration all non-elected claims under both the election of species requirement and the restriction requirement.

REJECTIONS UNDER 35 U.S.C. 102

Rejection of claims 1-5, 7-8, 10, 12, 14, 40-46, 49, 51, 55-56 under 35 U.S.C. 102(b) over the '478 patent

The Examiner has rejected independent claims 1, 40, 55, and 56, and dependent claims 2-5, 7-8, 10, 12, and 14, 41-46, 49, and 51 under 35 U.S.C. 102(b)

as being anticipated by the '478 patent. Specifically, the '478 patent discloses a metal-human growth hormone (M-hGH) complex contained in a polymer matrix for controlled delivery. Though there are nomenclature-based similarities between the instant application and the '478 patent, the structures of each are not the same. The '478 patent discloses the use of metal ions and exemplifies the use of Zn^{+2} to complex with human growth hormone (hGH), which uses +2 zinc valency for the complexation. See col. 2, ln. 37-58. Additionally, the Zn:hGH molar ratio range described in the '478 patent ranges from 4:1 to 100:1. See col. 2, ln. 51-54. The metal cation and the hGH are formulated in solutions in which each is at least slightly soluble and aqueous solutions are preferred. See col. 5, ln. 27-32. The process of preparing the Zn:hGH complex disclosed in the '478 patent follows the procedure of dissolving hGH in a sodium bicarbonate solution (pH 7.2) mixed with a solution made with deionized water and Zn-acetate dehydrate. See col. 8, ln. 1-9. This procedure was stated to form a Zn:hGH complex, which is directly formed as a result of soluble reagents allowing ionic coupling.

One difference between the '478 patent and the independent claims of the instant application is that '478 patent uses a soluble Zn-acetate dehydrate, which is in contravention to the use of a sparingly soluble particle (exemplified by an insoluble Zn-carbonate on pg. 25, ln. 5-15 of the present application). Zn-acetate dihydrate (which is exemplified in the '478 patent) has a solubility of 1g in 2.3 ml water, which is 1g in 2.3 grams of water. On the other hand, Zn-carbonate is only sparingly soluble at 0.001g in 100g of water. The use of a more soluble salt (such as in the '478 patent) allows for much more significant counter ion dissociation, and thus, provides for the complexation required by the '478 patent. As the zinc components between the '478 patent and the presently claimed invention are not equivalent, the use of one cannot

provide a basis for anticipation of the other. In other words, as the '478 patent does not teach the use of a sparingly soluble biocompatible particle as defined by the specification, there can be no anticipation. In other words, one skilled in the art would not interpret the term "sparingly soluble" to include those compositions taught or suggested by the '478 patent, as the '478 patent seeks complexation. Disassociation must occur before such zinc complexation can occur as taught by the '478 patent.

Further, the '478 patent does not teach the deposition of the hGH onto the sparingly soluble particle. Instead, as stated, the '478 patent teaches complexation between solubilized components. Thus, for this second independent reason, this reference is not believed to provide a basis for anticipation.

The process of manufacture of the '478 patent and the present invention also provides evidence that these separate inventions require distinctive results. The '478 patent uses the aforementioned Zn-acetate dihydrate dissolved into a solution, which results in free and individual Zn^{+2} ions able to complex by ionic association with another entity in solution. When the free and individually disperse solvated Zn^{+2} ions are admixed with a solution containing hGH, a complex between a Zn^{+2} ion and the hGH macrostructure is formed.

It should also be noted that the acceptable and disclosed molar ratios described in the '478 patent of Zn^{+2} and hGH ranged from 4:1 to 100:1, where zinc has a 65.4 Mw (Physical Chemistry: Fifth Edition, *The Periodic Table*, Peter Atkins, W.H. Freeman and Company, New York (1994)) and hGH has a 22,124 Mw (The Merck Index: Twelfth Edition, Editor Susan Budavari, pg. 1488, Merck Research Laboratories, Whitehouse Station, NJ (1996)). A conversion from mole ratios to weight ratios provides a zinc to hGH ratio from 0.01:1 to 0.29:1. Alternately, the

present invention includes a zinc particle to protein weight ratio of 1:10 to 100,000:1, indicating weighty insoluble particles as opposed to the solublized free Zn^{+2} ions. The large difference between the singular Zn^{+2} ions of the '478 patent compared to the larger insoluble particles required by dependent claims 2 and 41 is another indication, at minimum with respect to claim 2 and 41, that the '478 patent does not anticipate the presently claimed invention.

Although there are metals within the insoluble particles that may allow for association, the physiochemical process of formation results in a different and distinct product. Further, the Applicant is not claiming any incidental complexation that might occur if a few zinc ion, for example, become disassociated. Most "insoluble" salts are completely insoluble, but disassociate at such a low level, they are deemed to be insoluble. Thus, a complex formed between a metal ion and a protein is fundamentally different from a composition that results from depositing a protein onto an insoluble or sparingly soluble particle, even though that particle may contain the identified ion.

With respect to each of the pending independent claims, i.e., 1, 40, 55, and 56, all of these claims include a limitation that provides a sparingly soluble particle having a protein deposited thereon. As such, the above arguments are believed to be applicable to all of the pending independent claims. Thus, it is respectfully requested that the Examiners rejections related to claims 1-5, 7-8, 10, 12, 14, 40-46, 49, 51, 55-56 under 35 U.S.C. 102(b) by the '478 patent be withdrawn.

Rejection of claims 1, 5, 7-9, 40, 49, 50, and 52-56 under 35 U.S.C. 102(b) over the '980 patent

Claims 1, 5, 7-9, 40, 49, 50, and 52-56 were rejected under 35 U.S.C. 102(b) as being anticipated by the '980 patent. The '980 patent discloses the stabilization of porcine growth hormone (pGH) by association with porcine serum albumin (PSA) prior to incorporation into polymer matrix delivery devices. The '980 patent can optionally use a metal complex, such as zinc-porcine growth hormone complex (Zn-pGH). See col. 2, ln. 56-61. In these embodiments, the zinc is complexed with a pGH, which is physiochemically more similar to the process described by the '478 patent. Thus, the same arguments described above to distinguish the '478 patent from the instant claims are applicable here, and are incorporated herein. The '980 patent explains the zinc-protein complex to be derived is from a zinc recombinant porcine growth hormone, which would inform one skilled in the art that zinc ion is used. See col. 5, ln. 48-55. As stated, the use of a zinc ion consequentially results in a product formation similar to that of the '478 patent.

The '980 patent teaches of compositions formulated for stabilizing the pGH protein. This is accomplished by admixing a zinc recombinant porcine growth hormone with porcine serum albumin. The specification explicitly identifies the stabilizer by stating, "[a]ccording to the present invention, a stabilizing amount of porcine serum albumin (PSA) is mixed with porcine growth hormone prior to administration." See col. 2, ln. 20-25. Additionally, the '980 patent specification identifies that PSA "has been found to stabilize porcine grown hormone when admixed therewith in respective ratio within the range of from about 10:1 to about 1:4." See col. 2, ln. 67 to col. 3, ln. 2. Furthermore, the '980 patent is only directed to stabilizing pGH with PSA, and does not identify a pGH stabilized without PSA. Further, there is no evidence that the '980 patent teaches the deposition of a protein on a sparingly soluble particulate. Thus, for these alternative reasons, this reference is

believed to be inapplicable to the present claims, and the Applicants respectfully request withdrawal of this rejection.

OBVIOUSNESS-TYPE DOUBLE PATENTING

Rejections of claims 1, 7-13, 55, and 56 under the judicially created doctrine of obviousness-type double patenting over claims 1, 2, 6, 12, 18-21, 24, and 25 of the '588 patent

The Examiner cited claims 1, 2, 6, 12, 18-21, 24, and 25 of the '588 patent in making an obviousness-type double patenting rejection of claims 1, 7-13, 55, and 56 of the present application. A terminal disclaimer is filed herewith which is obviates the double patenting rejection. Withdrawal of this rejection is respectfully requested.

In view of the foregoing, Applicants believe that claims 1-14, 40-47, 49-56, and new claim 57, present allowable subject matter and allowance is respectfully requested. If any impediment to the allowance of these claims remains after consideration of the above remarks, and such impediment could be alleviated during a telephone interview, the Examiner is invited to telephone the undersigned attorney, or Gary Oakeson, at (801) 566-6633, so that such issues may be resolved as expeditiously as possible.

Dated this 20 day of March, 2003.

Respectfully submitted,

M. Wayne Western
Attorney for Applicant
Registration No. 22,788

THORPE NORTH & WESTERN
P.O. Box 1219
Sandy, UT 84091-1219
(801) 566-6633

AMENDMENT (marked-up version)

Please cancel claim 48.

Please add new claim 57 as follows:

57. (New) The method of claim 40 wherein said protein or peptide is selected from the group consisting of oxytocin, vasopressin, adrenocorticotropic hormone, epidermal growth factor, platelet-derived growth factor (PDGF), prolactin, luteinizing hormone releasing hormone (LHRH), LHRH agonists, LHRH agonists, growth hormone, growth hormone releasing factor, insulin, erythropoietin, somatostatin, glucagon, interleukin (including IL-2, IL-11, IL-12, etc.), interferon-α, interferon-β, interferon-γ, gastrin, tetragastrin, pentagastrin, urogastrone, secretin, calcitonin, enkephalins, endorphins, angiotensins, thyrotropin releasing hormone (TRH), tumor necrosis factor (TNF), parathyroid hormone (PTH), nerve growth factor (NGF), granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (GM-CSF), macrophage-colony stimulating factor (M-CSF), heparinase, vascular endothelial growth factor (VEG-F), bone morphogenic protein (BMP), hANP, glucagon-like peptide (GLP-1), renin, bradykinin, bacitracins, polymyxins, colistins, tyrocidine, gramicidins, cyclosporins, enzymes, cytokines, antibodies, vaccines, antibiotics, antibodies, glycoproteins, and combinations thereof.

No new matter has been added by virtue of these amendments.